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Seminar on Symposium on
Blood and its Derivatives
Cartagena, Colombia, 25-30 November 1984

# REPORT *

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## INTRODUCTION

Industrial production of plasma fractions started in the developed countries in the mid-forties after the first industrial method for the production of human albumin was developed in the United States.

At present, although blood is a renewable resource available in all countries of the world, almost the totality of blood fractions are produced in the developed countries. However, with the exception of the United States, which are the main and almost only exporter of plasma and blood derivatives, the rest of the countries still have to import a high percentage of their requirements in order to satisfy their internal demand.

From the point of view of commercialization and integration, fractionation industry shows very different characteristics. With few exceptions, namely Denmark, Sweden and the Red Cross, all companies have subsidiaries in several other industrialized countries. In general terms, they are involved in the process of commercialization, that is, extraction, transformation, distribution and marketing.

The market of blood derivatives is in the hands of a few companies located in the developed countries. The share of developing countries in the world production is only 10% as compared with 50% of the United States and 40% of Europe, Japan and Australia. It is therefore obvious that there exists a very wide gap which prevents the developing countries from meeting even a fraction of the demand for blood and derivatives. This is illustrated by the fact that the average consumption of albumin per one million inhabitants in some developing countries in North Africa is about 9 kg compared to 203 kg in Europe and 296 kg in the USA. The supplies of blood and blood fractions available to the developing countries are not adequate to cope with the needs of even 40% of the population of cities, and the situation in the rural areas is much worse.

In Latin America, with the exception of Brazil, Cuba and Mexico which are producing some of the stable derivatives, the rest of the countries depend entirely on imports for the provision of plasma fractions required for their health care programmes. There is an increasing interest in the Governments

of the region to improve the quality of transfusion services through the improvement of the scientifique and technical level of the programmes for blood collection. Significant efforts are being made to establish laws and regulations for the control of blood donations and the commercialization of blood and its derivatives. Blood transfusion services in Latin America have mainly been developed and are run by private blood banks, individual hospitals and local Red Cross Organizations. Blood is obtained in the countries of the Latin American region through voluntary donors (relatives of patients) and frequently from paid donors. However, in some countries, like Brazil, Mexico and Peru, commercialization of blood through paid donors is still playing a very important role in the obtention and collection of blood.

Except for the few countries producting plasma fractions, almost the totality of blood collected in the region is used mainly for transfusion of whole blood and for the separation of cellular blood components (mainly cell concentrates, platelets and fresh frozen plasma). In general, the blood collected in Latin American countries is of good quality. Storage conditions for whole blood, cell concentrates, fresh frozen plasma and cryoprecipitates are also satisfactory. Medical and paramedical personnel involved in all aspects of blood collection and fractionation is highly qualified. On the other hand it has been observed a lack of co-ordination between the numerous private blood banks existing in all the countries and the public blood condition units, hospitals and clinics.

The fractionation industry is a unique industry which requires efficient systems of collection and control, high investment (up to 10 million US$ for a sophisticated production plant) and last, but not least, deep knowledge of the different technologies involved.

In the light of the above and in compliance with its mandate viz "To promote and accelerate the industrialization of developing countries", UNIDO is committed to create a certain necessary and important awareness within the fold of the developing nations. Such awareness will encompass the problems of the industrial sector as well as their economic and social manifestations.

In September 1982, UNIDO, in co-operation with the Swedish Ministry of Health and Social Affairs organized an international "Seminar on National Self-Reliance in Blood and Blood Fractions for Developing Countries" with a view to acquainting representatives of developing countries with the various facets of blood transfusion services and the plasma fractionation industry. During the meeting a plan of action was prepared which included inter-alia the different actions that developing countries should consider at national, sub-regional and regional level.

At sub-regional/regional level it emerged from the discussions during the Seminar that it is crucial to train a large number of personnel from developing countries at all levels at different disciplines starting from blood collection, preservation to plasma fractionation. As it is not feasible to train such large numbers of personnel abroad, it was recommended to establish regional centres equipped with laboratory/pilot plant facilities for collection, preparation and fractionation thus combining all the relevant activities. Such a Centre can also take up activities for the development of technology thus creating the necessary infrastructure for the establishment of this kind of industry in the different regions.

In order to find ways and means for implementing these recommendations, UNIDO is organizing a series of regional meetings in Africa, Asia and Latin America. As a first step, UNIDO in cooperation with the Colombian Red Cross and the "Centre Nationale pour la Transfusion Sanguine" of France organised the "Latin American Symposium on Blood and its Derivatives".

During the Symposium, a report on the situation of this sector was presented followed by scientific and technical papers on different aspects on Blood and its Derivatives.

At the end, a "Plan of Action" was adopted unamimously by all participants including recommendations for follow-up action in the Latin American regions.

## ORGANIZATION OF THE MEETING

The Symposium, which was held in Cartagena, Colombia from November 25 to 30 was inaugurated by the Ministry of Health of Colombia, Dr. Amaury Garcia. Dr. Rueda Montaña, president of the Colombian Red Cross welcomed the delegates and expressed the importance of the Seminar for Colombia and for the Latin American countries. The UNIDO representative, Dr. A. Tcheknavorian, conveyed the greetings of the Executive Director of UNIDO to the participants and briefly presented UNIDO's programmes in the field of blood derivatives. She expressed her gratitude to the Colombian and French Governments for their co-operation and highlighted the importance of holding the Symposium in the Latin American regions as a fist step in a programme aimed at obtaining self-sufficiency in Latin America in the field of Blood and its Derivatives.

## PRECIS OF THE SYMPOSIUM

Twenty two international experts presented papers concerning various aspects of blood and its derivatives. After the presentation of papers, detailed discussions ensued. Summaries of the daily discussions and comments made which are relevant to the subject are given below.

REPORT FOR MONDAY, 26 NOVEMBER 1984

Morning: Chairmen: Dr. TCHEKNAVORIAN, Professor RUFFIE

Moderator: Dr. ROUGER

Rapporteur: Dr. ROUGER

Following the summary report presented by Dr. ROUGER (cf. official document) a number of questions and comments were put forward. Unfortunately, not all the names of the speakers were understood so that, in this respect, this document contains a considerable number of deficiencies and omissions for which the writer presents his sincere apologies.

Dr. ROUGER began by explaining and recalling the nature of the mission undertaken by UNIDO consultants. The mission consisted of an objective evaluation, or at least as objective as possible, based on reference criteria normally applied (and pre-established by UNIDO) to blood transfusion in the countries visited. After completing that evaluation, the consultants were to put forward recommendations which could serve as a basis for discussion in drafting specific proposals for consideration by UNIDO. As Dr. ROUGER stated, the philosophy of the mission demanded consultation with professional blood transfusion experts before any comment by the political authorities. The result was an absence of uniformity in the summary put forward as a basis for discussion at the symposium. A working session planned for Thursday, 29 November would make it possible to draw up a much more reliable document, since it would take account of medium and long-term needs and possible solutions.

Dr. GARRETA (CNTS - National Blood Transfusion Centre - Paris, France), speaking as French co-ordinator for Franco-Brazilian collaboration, recalled the fundamental principles for that collaboration which might possibly serve as a model. In 1981, Brazil decided to set up a blood transfusion development programme (PRO SANGUE, under the direction of Professor LUIS GONZAGA DOS SANTOS DE RECIFE), part of which relied on co-operation with France. The underlying principle of that co-operation was the twinning of a French transfusion centre with a Brazilian centre. Up to the present time, several twinnings had already given positive results. (Recife/Lille, Belem/Angers, Brasilia/Rennes).

Following Dr. GARRETA's intervention, and a reminder by the UNIDO representative of the need to be essentially constructive, there were a great many questions.

The representative of Venezuela expressed surprise that his country had not been mentioned for, in his opinion, it had been a model and example to Latin America for decades. There was an existing organic law, complete absence of paid donors, control of blood transfusion centres by the Ministry of Health, and so on. Dr. BRITO was likewise surprised that the use of placental blood should be advocated. Dr. GARRETA replied that the lack of venous plasma in a great many places fully justified that procedure.

A representative of Mexico associated himself with the preceding comments, since his country had had blood banks since 1962 and the preparation of new regulations was currently nearing completion. He also said that he had a report on blood transfusion in Mexico which he could make available to participants.

Dr. GONZAGA (Rio-Brazil), after commending the work of the consultant group, recalled that the PRO SANGUE programme would lead to the creation of 25 centres in Brazil and the elimination of paid donations. He also confirmed the extent to which Venezuela had for a long time been an example to Latin America.

Another representative of Mexico (the Director of social security blood transfusion centres) recalled the geographical difficulties which existed in America. He also recalled that there were still too many commercial transfusions and was concerned that there was only one supplier of plastic sacs, which was a financial limiting factor in the development of transfusion in his country.

A Peruvian participant (Lima) reported some facts on the situation in Peru. Although the consultants might have been able to see a few operational structures in Lima, there was a different situation in the country as a whole, which remained very short of blood transfusion services. The reason for this was the inadequate co-ordination and activity on the part of the Peruvian Red Cross. He earnestly requested French assistance in developing transfusion in his country.

Dr. TCHEKNAVORIAN said that, due to financial constraints, it had not been possible to visit some countries. The principal objective of the consultants was to investigate those countries which were the most lacking in blood transfusion facilities. She reiterated that the Thursday afternoon meeting would be essential in that it would permit the revision, expansion and refinement of the expert report. She also advocated that working groups to prepare for the Thursday meeting should be set up immediately.

Dr. VEJARANO (Colombia) thanked the German Red Cross for its assistance to his country. He took the opportunity to remind participants that the Cartagena Convention was to serve as a model. Those remarks were echoed by Dr. CALVO (Colombia), who pointed out that Colombia had passed an organic law in 1981. It was thanks to this law that the Colombian transfusion programme had reached a high standard including, among other things, immunohaematology and detection of hepatitis.

The representative of the Argentine Government said that there was a sector of industry in Argentina devoted to fractionation of human plasma. He added that the organic law of 1983 was being amended with respect to articles on the sale of blood and the role of the army in blood transfusion. He expressed his thanks to the consultants for the precision of their analysis.

Another representative of Venezuela reiterated that there were no professional donors in his country. He also said that the fact that there was only one firm selling plastic material was indeed, in his opinion, an economic tragedy.

The representative of Costa Rica broadly agreed with the content of the report, but regretted that the consultants had not had enough time. She pointed out that almost the entire population in her country was protected by social legislation, which was a matter of interest in the context of the symposium. Her Government was currently working to set up and develop mobile blood collection teams.

The Director of the Brazilian PRO SANGUE programme took the opportunity to recall the difficulties encountered in implementing the programme and stressed the need for constant determination, involving three ministries (health, education and social security). PRO SANGUE was currently developing the use of home produced plastic sacs.

The representative of Cuba said that 500,000 units of blood were collected each year, including 300,000 by people's organizations. His country was ready to give advice and participate in co-operative programmes.

Dr. REVIRON, recalling the four applications of transfusion, stated that in Latin America priority should first of all be given to components capable of reoxygenating the patient and restoring his circulating blood volume.

During the morning, Professor RAVAULT gave his lecture (cf. documents) followed by a presentation by Mr. Vico FRESIA (Milan), Secretary-General of the International Federation of Blood Donor Organizations (IFBDO). (The corresponding document is available from the Symposium secretariat.)

REPORT FOR MONDAY, 26 NOVEMBER 1984

Afternoon: Chairmen: Mrs. OSORIO, Mr. CAISSIAL

Moderator: Dr. GENETET

Rapporteur: Dr. GENETET

Following statements by Dr. GENETET (cf. document), Mr. CAISSIAL (President of the Fédération Française des Donneurs de Sang Bénévoles), * Dr. CHASSAIGNE and Dr. CAVALIER, there was discussion of a number of points of an ethical and technical nature. It is not possible to record them all. Suffice it to recall the intervention of Professor Charles MERIEUX, who expressed the view that books could be given to young blood donors without undermining the voluntary and unpaid character of donorship. He also suggested the introduction of a health card and the setting up of a blood bank for Latin America. 1/

The following themes also featured largely:

- Definition of voluntary and unpaid donorship,
- The problem of collection in the event of natural or other catastrophies,
- Equipment,
- People's organizations (Cuba),
- Role of the media,
- Methods of education in blood transfusion.

At the technical level, the presentations by Dr. CHASSAIGNE and Dr. CAVALIER both showed great personal and professional experience. They also spoke of the respect which should be given to the donor in order to ensure the subsequent supply of transfusions.

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* Translator's note: French Federation of Blood Donors.

1/ Statements by representatives of Colombia and Mexico are attached to this document.

REPORT FOR TUESDAY, 27 NOVEMBER 1984

Morning: Chairman: Dr. PICAZO

Moderator: Dr. GARRETTA

Rapporteur: Dr. CHASSAIGNE

Dr. PICAZO, Director of the Spanish Red Cross blood programme, presided over the meeting. He spoke briefly of transfusion in his country. Three major associations covered the whole country and, together with a number of other associations, were united in a large National Federation. It was regrettable that the lack of volunteer donors made it necessary to resort to some paid donors.

Dr. GARRETTA, with the aid of reproductions, gave a clear and precise presentation (see report) briefly setting out the nature of quality control at an establishment. It combined good manufacturing practices and good analysis permitting "in process" control. Dispatch authorization for the finished product was given by the quality control service after examining the relevant documents. If one of the major tests was not satisfactory, the product was rejected. If the overall error was very low, remaining within the method's margin of variation and relating to a test of minor importance, the General Management reviewed the file and might, in exceptional cases, authorize dispatch.

Dr. GARCIA (Mexico) reiterated the importance of quality control and of meeting standards laid down. He was in full agreement with the position regarding major tests, where product quality was suspect, but questioned the need for rejection when minor variations - within the method's margin of error - arose in tests of very secondary interest, and thought that in the latter event the product could be submitted to the General Management of the establishment supported by a fully argued case.

Dr. MONTERO (Costa Rica) asked a question on controls for non-stable products; he said that there were also standards for these, and they should be controlled. Quality assurance was a state of mind which should be present throughout the stages of collection, separation of blood components, tests, storage and distribution. Indeed, as Dr. CHASSAIGNE and Dr. CAVALIER had stated, written procedures for each stage should be drafted.

Professor AMBROISE THOMAS, in a clear, persuasive and well-documented presentation, reviewed the problems relating to the transmission of parasitical diseases (see report). This was a subject of particular concern and resulted in a great many questions (Colombia, Canada, Brazil, Cuba, China, Costa Rica and Venezuela).

Dr. MARTINEZ (WHO) said that one of his Organization's concerns was the fight against Chagas' disease. As an indication, he spoke of the 2,500 post-transfusion cases recorded in his country, which had a population of less than 10 million. He said that WHO could supply freeze-dried reagents for detection.

A delegate from CHINA gave an account of industrial pharmaceutical research in his country, devoted to the fight against malaria and the production of a new drug which could be injected intravenously. Professor AMBROISE THOMAS hoped that a derivative would soon be rendered more effective by procedures avoiding intravenous administration (extract of ARTEMISIA ANNUA-AUING HAO SHU).

The delegates of Cuba and Venezuela regretted that epidemiological supervision was sometimes scarce.

Dr. TCHEKNAVORIAN (UNIDO) pointed out that there was no miracle recipe and the object of the symposium must be a voluntary awareness by each of the participants of the need to develop productive capacity in order to resolve problems such as reagents or equipment (plastic sacs) by local means.

Dr. MARTINEZ introduced WHO actions in the field of blood transfusion and recalled that as early as 1979 the HIPOLITO UNANUE CONVENTION put forward the idea of a production centre for blood derivatives in Latin America, a scheme in which interest was confirmed in Bogota in April 1983.

WHO also announced a programme for reagents involving:

- Instituto de Salud Publica (Institute of Public Health), Chile
- Fio Cruz, Rio de Janeiro
- Instituto Adolfo Lutz (Adolfo Lutz Institute), Sao Paulo
- Gerencia General de Productos Biologicos (General Administration for Biological Products), Mexico.
- Instituto de Oncologia y Radiologia (Institute of Oncology and Radiology), Cuba
- Fundacion Polychaco (Polychaco Foundation), Argentina

He then gave a well documented lecture covering the AIDS situation in the world (see report). Four aspects from France were added by Dr. GRISCELLI:

- He had observed 11 cases of AIDS in children, in Paris, with different clinical symptomatology (absence of neutropenia and Kaposi's Sickness).
- Resistances or healthy carriers must exist since, for example, in the case of one carrier-mother, only one of her twins was affected.
- In post-transfusional cases, as well, not all patients were affected: for example, three thalassaemia patients received contaminated blood, two showed symptoms, which were in fact reversible, and one was contaminated.
- Finally, the antibody was present at the beginning and then disappeared.

A delegate from Brazil wondered whether it would be advantageous for each country to undertake, for example, its own production of cryoprecipitates.

Dr. ARANSON, with the aid of slides, spoke of possibilities of viral diseases being transmitted and particularly of products to combat them (see Dr. GERETTY's report).

There were a great many questions on that subject, including references to the advantage of manufacturing immunoglobulins from persons who had antibodies (Brazil). All the participants expressed their concern at the possibility of transmitting a virus through the plasma of particular individuals (Cuba) and questions were raised on the danger of sending plasma from one place to another with the consequent risk of thus spreading the virus.

Dr. MARTINEZ (WHO) thought that the advantages nevertheless outweighed the risks.

Mexico offered to make its experience of ultra-violet inactivation available to participants.

Afternoon: Chairmen: Dr. RODRIGUEZ TORIA
Dr. RODRIGUEZ MOYADO

Moderator: Professor SALMON

Rapporteur: Dr. CHASSAIGNE

Professor VIGNERON (France) spoke on the comparison between the ideal of artificial blood and the reality of oxygen carriers (see report).

A great many questions were raised: the effect on acid-base balance (Professor COUDERT); fluorocarbons, which carried carbon well, had no effects in that area, possibly haemoglobin in solution. Dr. VEJARANO (Colombia) wondered if clinical use could be made of flusol D.A. in cardiovascular surgery; Professor VIGNERON thought that the use of oxygen carriers to feed inactivated products would be a very good indication.

Professor TAYEAU was interested in the role of haemoglobin solutions on oncotic pressure, hence the interest in solutions of polymerized haemoglobin macromolecules.

Cuba recalled the harmful effect on donor recruitment of taking about artificial blood.

The problems concerning haemoglobin antigenicity were brougnt up, although neo-antigens may appear as a result of antigenics.

Professor SALMON, in a very informative lecture, reminded his audience of what was essential and useful in the field of erythrocytic immunohaematology. He put forward effective and flexible solutions which could be widely adapted (see report). Then Dr. ROUGER spoke of the future and how each country could make itself self-sufficient.

The remainder of the afternoon was devoted to the very many questions from the audience.

Dr. RODRIGUEZ MOYADO, at the request of Professor SALMON, traced the history of that activity in Mexico, made possible, as he emphasized, by the teaching of Professor SALMON 20 years before. He had developed a system for the manufacture of a panel which at first was kept deep frozen and now could be conserved for two months and distributed throughout the country. He had also introduced training for staff at various levels, which was open to the whole of Latin America. The system also now permitted the carrying out of interesting research on the distribution of groups in Mexico, for example.

Professor SALMON thanked Dr. RODRIGUEZ and reminded the audience that what had been done in Mexico could be applied elsewhere.

There followed a great many questions on frequencies of groups, antibodies, and the respective value of research into irregular agglutinins and compatibility tests in the laboratory.

On that latter point, Professor SALMON and Dr. ROUGER underlined the effect of errors and the importance of tests for ABO groups at the time of transfusion. Mexico was self-sufficient in ABO reagent and therefore hoped to apply those precautionary measures.

Finally, they answered questions on haemolytic disease in new-born infants. Professor SALMON emphasized the impossibility or extreme difficulty of immunological diagnosis, given the fact that they were dealing mainly with a hepatic disease.

As it was getting late, Professor SALMON felt obliged to close the meeting.

REPORT FOR WEDNESDAY, 28 NOVEMBER 1984

Morning: Chairman: Professor Luis Augusto GONZAGA DE RECIFE

Moderator:

Rapporteur: Mr. VALETTE

## Fractionation of plasma

Dr. Lucien MARTINACHE from the Transfusion Centre, LILLE (France) gave a presentation of traditional methods of producing stable derivatives. Ever since Cohn's first work in 1941, the same requirement for quality in the original plasma remained fundamental. It must be frozen in an hour. Unless that condition was met, it would only provide albumin.

Factor VIII and albumin were the two major products. Factor IX, fibrinogen, immunoglobulins were also produced. Products such as fibronectin, transferrin and somatomedin were being studied and could be extracted from plasma. Quality constraints, and also those of profitability, had to be respected. Seven tons of albumin were required in France every year.

The principal methods in use relied on variations in pH, temperature and ionic force, precipitation techniques using ethyl alcohol, and chromatographic filtration and ultrafiltration. Sodium caprylate was an essential stablizer allowing final inactivation at temperatures between 10° and 60°C. The industrial use of chromatography and ultrafiltration would make it ever more possible to obtain products of very high purity.

Dr. TCHEKNAVORIAN (UNIDO) then spoke of the fractionation industry in developing countries. After reminding her listeners of the traditional basic methods used in fractionating plasma, she listed those products which were of the greatest significance for public health and the quantities required for a given population. UNIDO, it was recalled, could assist in the training of staff in those fractionation technologies. The base material could be plasma or placenta. The geographical implantation of a fractionation industry depended upon co-operation between UNIDO and blood banks. Preliminary studies relating to the study of projects for implementation could be partly carried out by UNIDO experts, who were capable of providing initiation into the necessary techniques.

Dr. Jean-Louis TAYOT (MERIEUX Institute - FRANCE) then outlined new technologies used in the production of stable human blood derivatives. Chromatographic techniques were described: their application was based on the industrial separation of proteins. Specific techniques of chemical or immunological affinity chromatography were presented. Answering the question of why there had been such a delay in using them in blood fractionation, Dr. TAYOT explained that the Cohn method was proven and ethanol inactivated all viruses. He then showed the porous silica support which he used: 1,000 hectares of surface area for 300 kg of granules contained in an industrial separation column. The granules coated in DEAE Dextram made it possible to separate albumin and immunoglobulins by ionic charge. The reliability of that method was underlined by the extreme purity of the products obtained. It was an immunochromatographic technique which made it possible to purify or recover specific antibodies from a mixture. An installation for producing blood derivatives which did not include the use of chromatography in its various forms was inconceivable nowadays.

Dr. Francis MESNIER (Blood Transfusion Centre - Bordeaux - France) reported upon the activity of a Regional Centre representing a region of 4.5 million inhabitants. The Centre produced labile and stable derivatives from 45,000 litres of plasma per year, in addition to transfusion activities. Factor VIII was one of the products for which there was the greatest demand. It was therefore manufactured with the maximum possible yield. An automated industrial process was used to obtain albumin, factor IX and immunoglobulins, by thermocoagulation, ultrafiltration and chromatography.

## Discussion

The representative of Mexico emphasized that albumin requirements could not be covered by local production. Placentas would therefore be a goood source. Mr. TAYOT's presentation was therefore particularly welcome. In Mexico, a million placentas a year could be collected. Collections were organised by private companies. There should therefore be transfers of that technology even if the level of automation was lower.

Mr. TAYOT replied that once the installation was complete, its operation was straightforward. In addition, the content of the columns remained unchanged for 18 months: it was therefore economical in operation. The techniques were patented and could be licensed.

Dr. ARANSON (USA) pointed out that consumption of albumin in the United States of America was sometimes higher than really needed.

Professor TAYEAU asked what use was made of eliminated lipoproteins.

Dr. TAYOT replied that that was currently the subject of research.

Dr. MERIEUX repeated his offer for the installation of a centre for the South American continent where, as in the case of foot and mouth disease, collaboration between the State and private industry was possible, transfusion ethics being an incentive to devote the profits towards research of general concern.

Dr. TCHEKNAVORIAN said that a pilot installation would be needed in Latin America to test the various methods. It would also be essential to provide the necessary training for technicians.

The CHAIRMAN asked whether a pilot scheme with human plasma would pose an ethical problem.

Dr. ROUGER thought that there would be no ethical problem provided that the operation of the plant was fully public.

Dr. GENETET asked why it was necessary to obtain blood from donors when albumin could be obtained from placentas.

Dr. MARTINEZ SILVA said that tests, which were to be encouraged, were being carried out in Latin America, for example in Rio and Cuba. He asked what the position was relating to the propagation of herpes virus.

Dr. TAYOT said that there was no risk to be feared from placenta derivatives, since there had been no problem during 14 years of albumin production and more than 30 years of globulin production. Marker viruses had even been used to prove inactivation.

Dr. ALMA LUCIA (Colombian Red Cross - Bogota - Colombia) asked the origin of the placentas used in France.

Dr. TAYOT said they were collected in 30 countries throughout the world, incuding Europe, North America and Eastern Europe.

Mr. MARTIN said that placentas came from Europe, Canada and the United States of America. They did not come from developing countries. While a smaller installation was possible, for it to be profitable it required 1,000 tons or 1.6 million births per year.

Regarding the price of placentas, it required authorization from the nospital which asked for reimbursement of its costs. That came to about 50 cents per kg of placenta.

Mr. BALLESTER (Cuba) asked what filters were used with alcohol. He also asked what container was used for transporting albumin.

Dr. TAYOT said that ultrafiltration was possible with alcohol. There had been no problems with the placental albumin from the MERIEUX Institute. It was of course difficult to purify placental albumin.

Dr. MARTINACHE thought that more than two centres for the continent were needed, one centre for 30 million inhabitants.

Dr. BRAVO (Panama) was worried that the proposed equipment was too sophisticated.

Dr. BRITO (Venezuela) said that his technicians provided good service and maintenance for his cell separator. He needed reagents for measuring coagulation. He had produced a placental thromboplastin which seemed to him to be as good as that from the brain. But it contained haemoglobin.

Mrs. TCHEKNAVORIAN said that placental technology was still little known in developing countries. A pilot installation was certainly needed.

AFTERNOON

Dr. LOMBARD (Army Health Service) described his experience in lyophilization of albumin and the use of plastic sacs as containers. Asked how deep freezing was achieved, he said that sacs containing 300 ml of plasma were inflated with nitrogen. After freezing there was therefore an empty space. The sacs permitted a marked improvement in freezing and a life of 5 years.

Dr. SCHMITT (Federal Republic of Germany) spoke on the use of blood derivatives. Instead of always using whole blood, each patient could be given what he specifically required: albumin, immunoglobulin, coagulation factors. It was clear that albumin had a very important role in many cases, hence the increase in its consumption.

Dr. PERALTA (Guatemala) asked about transfusion of the patient's own blood, collected prior to surgery.

Dr. SCHMITT said that the method, called haemodilution, was widely practised in Germany, up to a haematocrit of 35 per cent.

Dr. PINO (Argentina) asked about the treatment of haemophilia using factor VIII in Germany.

Dr. SCHMITT was familiar with the situation only in his region. He used 70,700 units of factor VIII.

Dr. ARANSON, speaking on behalf of Dr. FINLAYSON, in answer to the question why plasma should be fractionated, said whole plasma was not appropriate for all treatments, particularly the treatment of haemophiliacs. Moreover, fractionated plasma was safer to use.

Dr. MENITOVE spoke of the utilization of factor VIII. There was one haemophiliac for every 6,000 persons, 80 per cent with haemophilia A, 10 per cent with haemophilia B and 5 per cent with Willebrand's.

Dr. TESSALO PINTO (Argentina) said that in his centre there were 1,000 haemophiliacs. 45 per cent were being treated with concentrates and 55 per cent with cryoprecipitates.

Dr. NESBAKKEN (Norway) spoke on the use of human albumin and identified the real therapeutic indications of the product. He presented an economic balance sheet of treatments using albumin. Intensive treatment should always be supported by precise diagnosis.

Professor GRISCELLI (Paris - France) gave details of medications for treatments using specific immunoglobulins. Heterologous serotherapy tests had lead to the use of serums from convalescent subjects, then to the extraction of specific immunoglobulins. The last stage was the intravenous use of those globulins. Immunoglobulins IgG 1, 2, 3 and 4 were monomers, and IgM were pentamers. There were standard immunoglobulins and specific globulins, whether of plasmatic or placental origin. The main indications were immune deficiencies. Indications for specific globulins were also detailed.

Dr. PINTO (Argentina) said that intravenous globulins were increasingly being recommended for AIDS for example. He asked Professor Griscelli's opinion.

Professor GRISCELLI said that it was indeed a powerful weapon in combating immune deficiencies, better than interferon.

Professor COUDERT asked if any information was available on active transfers of globulin from plasma and on transplacental transfers.

Professor GRISCELLI said that little was known on plasma transfer into tissue. There had been full-term births with a low level of immunoglobulins due to an abnormal placenta.

REPORT FOR THURSDAY, 29 NOVEMBER 1984

Morning: Chairman: Dr. CALVO

Moderator: Dr. ROUGER

Rapporteur: Dr. ROUGER

The morning was devoted to consideration of the socio-economic aspects and the infrastructures relating to blood transfusion in Latin American countries.

Professor SEIDL, President of the International Blood Transfusion Society, introduced that learned society and offered its assistance in implementing future projects.

Dr. CALVO presented a report on the technico-economic aspects and the infrastructure relating to blood transfusion in the countries of the Andean Regional Pact. The uncompromising report had international implications regarding blood and its derivatives.

Mr. MARTIN gave a brief outline of possible synergism between public and private organizations involved in the industrial processing of blood.

Professor SEIDL stated the broad outlines of a national blood programme for the Latin American countries.

Dr. GENETET recalled the rules regarding collecting blood from voluntary, unpaid donors.

Dr. ROUGER introduced the discussion points for the afternoon, when the Latin American participants would be protagonists:

- Collection of plasma,
- Problems related to the collection of placenta and its presentation to the public,
- Industrial policy applied to blood: fractionation, production of reagents, production of plastic,
- Collaboration between private and public bodies,
- Economic aspects of such industrial policy,
- Development of 'National Blood Programmes',

- Collaboration with international bodies,

- The problem of the treatment of haemophiliacs.

The afternoon was devoted to the presentation, by the representatives of Latin America, of their thoughts and proposals which are reflected in the Cartagena Plan of Action set out on page 15 and which was unanimously approved by all participants on the final day of the Symposium, Friday, 30 November.

## Cartagena Plan of Action

### INTRODUCTION

Blood and its derivatives are an essential component of health programmes. Their availability is vital if developing countries are to achieve the objectives which they have set for themselves in the field of health. However, the market for blood derivatives is in the hands of a few companies based in the developed countries. The share of developing countries in world production is only 10 per cent, compared with 50 per cent for the United State of America and 40 per cent for Europe, Japan and Australia. It is thus clear that there is an enormous disparity preventing developing countries from meeting even part of the demand for blood and blood derivatives. This is shown by the fact that the average consumption of albumin per million inhabitants in some developing countries in North Africa is in the region of 9 kg, compared with 203 kg in Europe and 296 kg in the United States of America. Supplies of blood and plasma fractions available in developing countries are insufficient to meet even 40 per cent of the needs of the urban population, and the situation in rural zones is much worse.

Countries in Latin America, with the exception of Brazil, Cuba and Mexico which produce some stable derivatives, depend wholly on imports for the plasma fractions needed in their respective health programmes. A growing interest can be seen among Governments in the region in improving the quality of transfusion services by raising the technical and scientific level of blood collection programmes.

The Lima Declaration and Plan of Action regarding UNIDO's role in industrial development provides that UNIDO shall be responsible for establishing the basic principles of industrialization and defining ways in which the international community can adopt measures in the sphere of industrial development aimed at creating a New International Economic Order. Resolution 28 states that the share of developing countries in world industrial production must be increased to a level of at least 25 per cent by the year 2000.

The WHO Alma Ata Declaration relating to primary health care recommends the achievement of "Health for all by the year 2000".

Bearing in mind the foregoing and considering:

(1) That blood and its derivatives are biological products of human origin for therapeutic purposes and consequently its commercialization is condemned;

(2) That many of these biological products have to be purchased by developing countries on the international* market at high costs with a consequent loss of foreign exchange;

(3) That the operation of national blood programmes requires reagents and inputs which also have to be bought on the international market at high cost, thus depriving these programmes of financial resources;

(4) That the effective operation of national blood programmes requires qualified personnel;

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* Translator's note: Original Spanish is "nacional" which appears to be an editing error.

(5) That in the Latin American region there are centres with recognised experience in the various branches of blood programmes related to blood transfusion including, inter alia, promotion, management, fractionation and manufacture of reagents;

(6) That diseases such as Chagas' disease and malaria are of significant importance in the Latin American region;

The Latin American group of countries recommends:

(1) The introduction of clear policies and legislation relating to blood and its derivatives in those countries which so far have none. In order to achieve this objective it is recommended that a National Blood Commission should be set up in all countries of the region, where necessary, to promote, co-ordinate and direct blood programmes in each country.

(2) The establishment of a Latin American network of centres working on the various aspects of the use of blood and its derivatives, bearing in mind the different levels of development reached by countries in the region.

- An ongoing exchange of information on the current situation relating to the production of reagents and inputs to industry in this field, existing capacity in terms of production of raw materials, quality control, and levels of technological development and production achieved.

- Organization of meetings of experts.

- Promotion of development in local industry for the production of reagents and inputs such as transfusion equipment and plastic sacs, etc.

- Training of human resources in areas such as administration and technical, scientific and financial aspects related to the blood and blood derivatives industry.

- Establishment of reference centres for quality control of products manufactured in the region. This will require the collaboration of international bodies such as UNIDO, PAHO and WHO.

- Offer of training programmes and/or visits by groups of persons in the region to a centre within the zone or outside it.

In order to implement these actions it will be necessary to set up a co-ordinating centre to take charge of organization, programming and the search for financing of development in line with the proposed objectives.

(3) It is considered important that industrial pilot projects should be developed. The establishment of a pilot plant is recommended where it will be possible to evaluate economic aspects of production, design, engineering, appropriate technologies, quality control and personnel training. This will require the support of Governments in the area, UNIDO and PAHO.

In this context it might be possible to develop technico-economic models for the production of blood derivatives covering various levels of production, for example, from:

100 to 400 litres/week

400 to 1,000 litres/week

1,000 to 2,000 litres/week.

(4) In order to develop national industry and improve technological capacity aimed at self-sufficiency, representatives of Latin American countries recommend Governments in the region to give special consideration to the need to stimulate the development of the blood industry, its derivatives, and its reagents and inputs. This includes preferential rates for imported inputs together with economic and financial incentives.

(5) The organization of a meeting with the object of defining the best methods of evaluating and preventing diseases which can be transmitted through transfusions such as malaria and Chagas' disease, relating research to the industrial potential locally available in each country.

This meeting should be preceeded by the visit of an Evaluation Commission, similar to that undertaken by UNIDO, which should begin its work as soon as possible.

(6) In order to accelerate the implementation of the Regional Plan approved by the Ministers of Health of the American countries in 1983, and allow the provision of efficient and effective national blood transfusion services by 1990, UNIDO should liaise with PAHO and other international and subregional organizations such as the International Red Cross and the International Blood Transfusion Organization, and with industrialized countries represented at this Symposium such as Italy, Germany, France and Austria in implementing the Plan of Action.

(7) UNIDO should make submissions for the consideration of the respective Governments of the region and subsequently organize an intergovernmental meeting in order to obtain political approval for the Plan of Action.

(8) That the Cruz Colombiana should initiate and co-ordinate the proposed network.

(9) That the Plan of Action should be called "Cartagena Plan of Action".

(10) That similar meetings should be held on blood and its derivatives in Africa and Asia.